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EXAMINER	
HUYNH, PHUONG N	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 09/08/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/914,088	DYSON ET AL.	
	Examiner	Art Unit	
	Phuong Huynh	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *Three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 June 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *42 and 44-86* is/are pending in the application.

4a) Of the above claim(s) *44-50,53-57 and 68-83* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *42, 51-52, 58-67 and 84-86* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 42, and 44-86 are pending.

2. Claims 44-50, 53-57 and 68-83 stand withdrawn from further consideration by the examiner, 37 C.F.R. 1.142(b) as being drawn to non-elected inventions.

3. Claims 42, 51-52, 58-67 and 84-86, drawn to drawn to an isolated peptide comprising SEQ ID NO: 1, are being acted upon in this Office Action.

4. In view of the amendment filed 6/21/04 and 5/24/04, the following rejections remain.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 42, 51-52, 58-67 and 84-86 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling only for (1) a peptide consisting of an isolated surface exposed epitope of the Cε2 domain of IgE wherein the surface exposed epitope consisting of Cε2 is P1 (SEQ ID NO: 1), (2) The said peptide wherein the isolated epitope is derived from a loop structure of the Cε2 domain of IgE, (3) The said peptide wherein the loop structure of the Cε2 domain of IgE is a A-B or a C-D loop, (4) An immunogenic composition the treatment of allergy comprising the peptide of SEQ ID NO: 1 and a carrier, (5) An immunogenic composition the treatment of allergy comprising the peptide of SEQ ID NO: 1 wherein the peptide is conjugated to a carrier, (5) The said immunogenic compositions mentioned above wherein the peptide is presented within the primary sequence of the carrier, (6) A vaccine for treatment of allergy comprising any the immunogenic composition mentioned above further comprising an adjuvant, (7) an immunogenic composition for the treatment of allergy comprising the peptide consisting of SEQ ID NO: 1 fused to a carrier molecule, (8) The immunogenic composition mentioned above wherein the peptide is presented within the primary sequence of the carrier and (9) a vaccine for the treatment of allergy comprising the immunogenic composition comprising the peptide consisting of SEQ ID NO: 1 wherein the peptide is expressed as a fusion protein and a carrier

molecule and an adjuvant, **does not** reasonably provide enablement for *all* peptide or *all* "mimotope thereof" of less than 100 amino acids in length "comprising" an isolated surface exposed epitope of the Cε2 domain of IgE, wherein said surface exposed epitope of Cε2 is SEQ ID NO: 1, (2) any immunogenic composition (claims 58-62, 84-86) or vaccine (claims 63-67) for the treatment of allergy comprising any peptide, any mimotope thereof of less than 100 amino acids in length "comprising" an isolated surface exposed epitope of the Cε2 domain of IgE, wherein said surface exposed epitope of Cε2 is SEQ ID NO: 1 and a carrier molecule (claims 58, 84) such as Protein D or Hepatitis B core antigen (claim 59), wherein the immunogenic composition is a chemical conjugate of the peptide or mimotope thereof (claim 60) or wherein the peptide or mimotope is presented within the primary sequence of any carrier (claims 61-62 and 85) or expressed as a fusion protein (claims 84) and further comprising an adjuvant (claims 63-67 and 86). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in **scope** with these claims.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention. The specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation.

The specification discloses only a peptide consisting of SEQ ID NO: 1 wherein the peptide is an isolated surface exposed epitope P1 of the Cε2 domain of IgE and the mimotope of SEQ ID NO: 1 is selected from the group consisting of SEQ ID NO: 8-9, 10-28, and 192-193 as shown on page 9. The said peptide and mimotopes are either conjugated to a carrier protein such as BSA or fused to HepB core protein for inducing anti-IgE antibody for treating allergy. The specification defines mimotope may be a peptidic or non-peptidic, or may have a sequence which differs from the native epitope but may also be exactly the same sequence as the native epitope. Although the two molecules share the same sequence, the mimotope will not presented in the context of the whole Cε2 domain structure, as such the mimotope may take a slightly different conformation to the native IgE epitope (page 5, lines 18-25).

The specification does not teach how to make *all* peptide and *all* mimotope thereof of less than 100 amino acids in length because the term "comprising" is open-ended. It expands the peptide and the mimotope thereof to included additional amino acids at either or both ends. There is insufficient guidance as to which amino acids to be added and whether the resulting peptide and mimotope would maintain its binding specificity IgE, in turn, would induce IgE specific antibody useful as a vaccine for the treatment of allergy. Given that SEQ ID NO: 1 is only 9 amino acids in length, the rest of the 90 amino acids are not adequately teach in the specification as filed. Further, there is insufficient in vivo working example demonstrating that any peptide less than 100 amino acids in length is effective for inducing IgE specific antibody useful as a vaccine for the treatment of allergy. Since the two dimensional structure of the peptide is not enabled, it follows that the 3D mimic epitope or mimotope of said peptide is not enabled.

Stryer *et al*, of record, teach that a protein is highly dependent on the overall structure of the protein itself and that the primary amino acid sequence determines the conformational of the protein (See enclosed appropriate pages).

Ngo *et al* teach that the amino acid positions within the polypeptide/protein that can tolerate change such as conservative substitution or no substitution, addition or deletion which are critical to maintain the protein's structure/function will require guidance (See Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure Prediction, pp. 492-495).

Skolnick *et al* teach that squence-based methods for function prediction are inadequate and knowing a protein's structure does not necessary tell one it's function (See entire document, Abstract in particular).

Abaza *et al* teach that even a single amino acid substitution outside the antigenic site can exert drastic effects on the reactivity of a protein with monoclonal antibody against the site (See abstract, in particular). Given the indefinite number of undisclosed peptide and mimotope, it is unpredictable which undisclosed peptide and mimotope would be useful for generating anti-IgE antibody that in turn would be useful for a vaccine against allergy. In fact, the specification discloses that "whether or not an antibody is anaphylactopgenic depends on the location of the target epitope on the IgE molecule ...based on the present state of knowledge, there is little or no predictability of what characteristics any antibody may have and whether or not it might have a positive or negative clinical effect on a patient" (see paragraph bridging page 2 to 3 of specification). Since the peptide and mimotope thereof are not enabled, it follows the peptide or

mimotope is conjugated to any carrier or fused to any carrier or within the primary sequence of any carrier in an immunogenic composition or in a vaccine are not enabled.

For these reasons, it would require undue experimentation of one skilled in the art to practice the claimed invention. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

In re wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), the decision of the court indicates that the more unpredictable the area is, the more specific enablement is necessary. In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take an undue amount of experimentation for one skilled in the art to practice the claimed invention.

Applicants' arguments filed 6/21/04 have been fully considered but are not found persuasive.

Applicants' position is that Claim 1 covers a peptide comprising a region of P1 (SEQID NO. 1), in which the peptide must be less than 100 amino acids (support for this amendment is found on page 14, line 10 of the specification). It is believed that none of the prior art disclose such peptides, nor a possible use for these peptides, and this claim is novel and inventive. The term "mimotope" is very well known and has a specific meaning that is clear to a man skilled in the arts and is fully defined on pages 5 & 6 of the present specification. A mimotope is a 3 D structure that mimics an epitope; for the artisan, identifying such mimics is a matter of using straightforward, well-documented methods, some of which have been highlighted on page 6 of the specification.

In contrast to applicant's assertion that a man skilled in the arts is able to make and use the claimed peptide and mimotope, as discussed above, the specification does not teach how to make *all* peptide and *all* mimotope thereof of less than 100 amino acids in length because the term "comprising" is open-ended. It expands the peptide and the mimotope thereof to included additional amino acids at either or both ends. There is insufficient guidance as to which amino acids to be added and whether the resulting peptide and mimotope would maintain its binding specificity IgE, in turn, would induce IgE specific antibody useful as a vaccine for the treatment of allergy. Given that the surface exposed epitope of SEQ ID NO: 1 is only 9 amino acids in length, the rest of the 90 amino acids are not adequately teach in the specification as filed. Further, there is insufficient in vivo working example demonstrating that any peptide less than

100 amino acids in length is effective for inducing IgE specific antibody useful as a vaccine for the treatment of allergy. Since the two dimensional structure of the peptide is not enabled, it follows that the 3D mimic epitope or mimotope of said peptide is not enabled.

7. Claims 42, 51-52, 58-67 and 84-86 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The specification does not reasonably provide a **written description** of *all* peptide or *all* "mimotope thereof" of less than 100 amino acids in length "comprising" an isolated surface exposed epitope of the Cε2 domain of IgE, wherein said surface exposed epitope of Cε2 is SEQ ID NO: 1, (2) any immunogenic composition (claims 58-62, 84-86) or vaccine (claims 63-67) for the treatment of allergy comprising any peptide, any mimotope thereof of less than 100 amino acids in length "comprising" an isolated surface exposed epitope of the Cε2 domain of IgE, wherein said surface exposed epitope of Cε2 is SEQ ID NO: 1 and a carrier molecule (claims 58, 84) such as Protein D or Hepatitis B core antigen (claim 59), wherein the immunogenic composition is a chemical conjugate of the peptide or mimotope thereof (claim 60) or wherein the peptide or mimotope is presented within the primary sequence of any carrier (claims 61-62 and 85) or expressed as a fusion protein (claims 84) and further comprising an adjuvant (claims 63-67 and 86).

The specification discloses only a peptide consisting of SEQ ID NO: 1 wherein the peptide is an isolated surface exposed epitope P1 of the Cε2 domain of IgE and the mimotope of SEQ ID NO: 1 is selected from the group consisting of SEQ ID NO: 8-9, 10-28, and 192-193 as shown on page 9. The said peptide and mimotopes are either conjugated to a carrier protein such as BSA or fused to HepB core protein for inducing anti-IgE antibody for treating allergy. The specification defines mimotope may be a peptidic or non-peptidic, or may have a sequence which differs from the native epitope but may also be exactly the same sequence as the native epitope. Although the two molecules share the same sequence, the mimotope will not presented in the context of the whole Cε2 domain structure, as such the mimotope may take a slightly different conformation to the native IgE epitope (page 5, lines 18-25).

With the exception of the specific peptide and peptide mimotope mentioned above, there is inadequate written description about the structure associated with function of *all* peptide and *all*

"mimotope" thereof of less than 100 amino acids in length because the term "comprising" is open-ended. It expands the peptide and the mimotope thereof to included additional amino acids at either or both ends. There is inadequate written description about which amino acids to be added and whether the resulting peptide and mimotope would maintain its binding specificity IgE, in turn, would induce IgE specific antibody useful as a vaccine for the treatment of allergy. Given that the surface exposed epitope of SEQ ID NO: 1 is only 9 amino acids in length, the rest of the 90 amino acids are not adequately teach in the specification as filed. Since the two dimensional structure of the peptide is not adequately described, it follows that the 3D mimic epitope or mimotope of said peptide is not adequately described.

In re Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111 indicates that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Finally, the specification discloses only one P1 peptide consisting of SEQ ID NO: 1 from human, a fusion protein comprising SEQ ID NO: 1 fused to a carrier selected from the group consisting of Protein D or Heatitis B core antigen. Given the lack of a written description of *any* additional representative species of peptide or mimotope thereof of less than 100 amino acids in length, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus. *See University of California v. Eli Lilly and Co. 43 USPQ2d 1398; University of Rochester v. G.D. Searle & Co., 69 USPQ2d 1886 (CA FC2004).*

Applicant is directed to the Final Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Applicants' arguments filed 6/21/04 have been fully considered but are not found persuasive.

Applicants' position is that Claim 1 covers a peptide comprising a region of P1 (SEQID NO. 1), in which the peptide must be less than 100 amino acids (support for this amendment is found on page 14, line 10 of the specification). It is believed that none of the prior art disclose such peptides, nor a possible use for these peptides, and this claim is novel and inventive. The term "mimotope" is very well known and has a specific meaning that is clear to a man skilled in

the arts and is fully defined on pages 5 & 6 of the present specification. A mimotope is a 3 D structure that mimics an epitope; for the artisan, identifying such mimics is a matter of using straightforward, well-documented methods, some of which have been highlighted on page 6 of the specification.

However, the specification does not reasonably provide a **written description** of *all* peptide or *all* "mimotope thereof" of less than 100 amino acids in length "comprising" an isolated surface exposed epitope of the Cε2 domain of IgE, wherein said surface exposed epitope of Cε2 is SEQ ID NO: 1, (2) any immunogenic composition (claims 58-62, 84-86) or vaccine (claims 63-67) for the treatment of allergy comprising any peptide, any mimotope thereof of less than 100 amino acids in length "comprising" an isolated surface exposed epitope of the Cε2 domain of IgE, wherein said surface exposed epitope of Cε2 is SEQ ID NO: 1 and a carrier molecule (claims 58, 84) such as Protein D or Hepatitis B core antigen (claim 59), wherein the immunogenic composition is a chemical conjugate of the peptide or mimotope thereof (claim 60) or wherein the peptide or mimotope is presented within the primary sequence of any carrier (claims 61-62 and 85) or expressed as a fusion protein (claims 84) and further comprising an adjuvant (claims 63-67 and 86).

The specification discloses only a peptide consisting of SEQ ID NO: 1 wherein the peptide is an isolated surface exposed epitope P1 of the Cε2 domain of IgE and the mimotope of SEQ ID NO: 1 is selected from the group consisting of SEQ ID NO: 8-9, 10-28, and 192-193 as shown on page 9. The said peptide and mimotopes are either conjugated to a carrier protein such as BSA or fused to HepB core protein for inducing anti-IgE antibody for treating allergy. The specification defines mimotope may be a peptidic or non-peptidic, or may have a sequence which differs from the native epitope but may also be exactly the same sequence as the native epitope. Although the two molecules share the same sequence, the mimotope will not presented in the context of the whole Cε2 domain structure, as such the mimotope may take a slightly different conformation to the native IgE epitope (page 5, lines 18-25).

With the exception of the specific peptide and peptide mimotope mentioned above, there is inadequate written description about the structure associated with function of *all* peptide and *all* "mimotope" thereof of less than 100 amino acids in length because the term "comprising" is open-ended. It expands the peptide and the mimotope thereof to included additional amino acids at either or both ends. There is inadequate written description about which amino acids to be added and whether the resulting peptide and mimotope would maintain its binding specificity

IgE, in turn, would induce IgE specific antibody useful as a vaccine for the treatment of allergy. Given that the surface exposed epitope of SEQ ID NO: 1 is only 9 amino acids in length, the rest of the 90 amino acids are not adequately teach in the specification as filed. Since the two dimensional structure of the peptide is not adequately described, it follows that the 3D mimic epitope or mimotope of said peptide is not adequately described.

In re Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111 indicates that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Finally, the specification discloses only one P1 peptide consisting of SEQ ID NO: 1 from human, a fusion protein comprising SEQ ID NO: 1 fused to a carrier selected from the group consisting of Protein D or Heatitis B core antigen. Given the lack of a written description of *any* additional representative species of peptide or mimotope thereof of less than 100 amino acids in length, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus. *See University of California v. Eli Lilly and Co. 43 USPQ2d 1398; University of Rochester v. G.D. Searle & Co., 69 USPQ2d 1886 (CA FC2004).*

Applicant is directed to the Final Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 42, 51-52, 58, 60, 63, 65, 84 and 86 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 93/05810 (April 1993, PTO 892).

The WO 93/05810 publication teaches various peptides such as rat or human IgE CH2-CH3, and mutated form thereof (mimotope) which comprise an isolated Cε2 domain of IgE as a vaccine for treating allergy (See abstract, claims 1 and 5 of WO 93/05810, page 14, in particular).

The reference peptide is 76 amino acids in length (See page 1, 31, in particular). The IgE Cε2 domain of the reference peptide inherently contains the surface exposed epitope (solvent accessible). The term comprising is open ended. It expands the claimed peptide of SEQ ID NO: 1 to read on the reference peptide. The WO 93/05810 publication further teaches an immunogen such as the reference peptide optionally conjugated (coupled) or fused to a heterologous carrier protein such as GST and optionally with an adjuvant such as alum (See abstract, claim 1 and 2 of WO 93/05810, page 7, line 32, in particular). Claims 51-52 are included in this rejection because the AB or CD loop structure is an inherent structure of the IgE constant domain to which the reference peptide is obtained. Thus, the reference teachings anticipate the claimed invention.

Applicants' arguments filed 6/21/04 have been fully considered but are not found persuasive.

Applicants' position is that Claim 42 has been amended to read on a peptide comprising a region of P1, in which the peptide must be less than 100 amino acids (support for this amendment is found on page 14, line 10 of the specification). It is believed that none of the prior art disclose such peptides, nor a possible use for these peptides, and this claim is novel and inventive.

However, the WO 93/05810 publication teaches various peptides such as rat or human IgE CH2-CH3, and mutated form thereof (mimotope) which comprise an isolated Cε2 domain of IgE as a vaccine for treating allergy (See abstract, claims 1 and 5 of WO 93/05810, page 14, in particular). The reference peptide is 76 amino acids in length which is less than 100 amino acids in length (See page 1, 31, in particular). Further, the term "Comprising" is open-ended. It expands the peptide to include additional amino acids at either or both ends so long the peptide has the surface exposed epitope of Cε2.

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 103(a) that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. This application currently names joint inventors. In considering Patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to

the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 42, 58, 59, and 60- 67 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 93/05810 (April 1993, PTO 892) in view of Ulrich *et al* (Adv Virus Res 50:141-82, 1998; PTO 892) or US Pat No 4,593,002 (June 1986; PTO 892)

The teachings of the WO 93/05810 publication have been discussed supra.

The claimed invention in claim 59 differs from the teachings of the references only that an immunogen wherein the carrier molecule is Hepatitis B core antigen or Protein D.

The claimed invention in claims 61 and 62 differs from the teachings of the references only that an immunogen wherein the peptide or peptide mimotope is presented within the primary sequence of the carrier.

The claimed invention in claims 64, 66 and 67 differs from the teachings of the references only that the vaccine for treatment of allergy comprising an immunogen comprising a peptide or mimotope wherein the immunogen is a chemically conjugate of the peptide or the mimotope or wherein the immunogen is expressed as a fusion protein and further comprising an adjuvant.

Ulrich *et al* teach that core protein of hepatitis B (HbcAg) is useful as an immunogenic antigen carrier since up to 40 amino acid residues at the N terminus, 50 or 100 amino acids in the central immunodominant c/e1 epitope region of HbcAg and up to 100 or even more residues at the C terminus can be inserted without interfering particle formation (See abstract, in particular). Ulrich *et al* teach that when applied together with adjuvant or even without adjuvant, such chimeric particles induced B and T cell immune responses against the inserted epitopes (See abstract, in particular).

The '002 patent teaches the use of various carrier such as protein D for vaccine composition to enhance immunogenicity of any immunogen (See entire document, column 4, line 41-45, in particular). The '002 patent teaches that the peptide is inserted within the primary sequence of the carrier in such as way that the peptide or protein of interest is exposed to the outside of the phage coat and accessible to the immune system of the vaccinated host (See column 8, in particular). The '002 patent teaches that the advantage of carrier is that it functions

for enhance immunogenicity, providing protein stability and retains the ability to replicate while the incorporated protein segment has the potential for inducing the specific immune response (See column 2, lines 55-62, in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to conjugate or to fuse any peptide or mimotope of interest such as the peptide as taught by the WO 93/05810 publication with a carrier such as the Hepatitis B core antigen as taught by Ulrich et al or the Protein D of Haemophilus influenza as taught by Mustafa *et al* where the peptide or peptide mimotope is within the primary sequence of the carrier as taught by Ulrich et al for a vaccine comprising said peptide, said carrier and an adjuvant as taught by the WO 93/05810 publication, Ulrich *et al* and/or Mustafa *et al.* From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art would have been motivated to do this because Ulrich *et al* teach that core protein of hepatitis B (HbcAg) is useful as an immunogenic antigen carrier since 50 or 100 amino acids of any peptide can be inserted in the central immunodominant c/e1 epitope region of HbcAg and such chimeric particles induced B and T cell immune responses against the inserted epitopes (See abstract, in particular). The '002 patent teaches that the advantage of carrier is that it functions for enhance immunogenicity, providing protein stability and retains the ability to replicate while the incorporated protein segment has the potential for inducing the specific immune response (See column 2, lines 55-62, in particular).

Applicants' arguments filed 6/21/04 have been fully considered but are not found persuasive.

Applicants' position is that Claim 42 has been amended to read on a peptide comprising a region of P1, in which the peptide must be less than 100 amino acids (support for this amendment is found on page 14, line 10 of the specification). It is believed that none of the prior art disclose such peptides, nor a possible use for these peptides, and this claim is novel and inventive.

However, the WO 93/05810 publication teaches various peptides such as rat or human IgE CH2-CH3, and mutated form thereof (mimotope) which comprise an isolated Cε2 domain of IgE as a vaccine for treating allergy (See abstract, claims 1 and 5 of WO 93/05810, page 14, in particular). The reference peptide is 76 amino acids in length which is less than 100 amino acids in length (See page 1, 31, in particular). Further, the term "Comprising" is open-ended. It

expands the peptide to include additional amino acids at either or both ends so long the peptide has the surface exposed epitope of Cε2.

13. No claim is allowed.

14. **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a).

Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phuong Huynh "NEON" whose telephone number is (571) 272-0846. The examiner can normally be reached Monday through Friday from 9:00 am to 5:30 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The IFW official Fax number is (703) 872-9306.

16. Any information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Phuong N. Huynh, Ph.D.
Patent Examiner, Tech Center 1600
September 3, 2004

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